Proceedings of ICBioMed 2025 Symposium: AI for Healthcare: Advanced Medical Data Analytics and Smart Rehabilitation
DOI: 10.54254/2753-8818/2025.AU27426

Can Nanotechnology Improve the Drawbacks of Deep-Sea Fish Oil?

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Abstract. Deep sea fish oil is widely used in preventing chronic diseases such as cardiovascular disease. However, due to the low-melting, hydrobility, oxidation, side effects also appears to be serious, such as poisoning and bleeding may occur. Besides, the bioavailabililty of deep sea fish oil.is also low. At present, with the increasing popularity of nanotechnology, new functional foods developed through nano encapsulation or delivery technology have emerged in the fields of food safety and research and development (with significantly reduced side effects and significantly improved bioavailability). However, it's still unclear that which nanotechnoly is the most efficient way to solve the unmet medical needs of deep fish oil. Therefore, this article aims to investigate the application of several different nanotech in improving deep sea fish oil, and discuss the feasibility of using nanotechnology to improve the high melting point, easy oxidation, and hydrophobicity of deep-sea fish oil from the preparation and purification steps. Through investigation, this thesis found that nano lotion is the most effective way to improve the drawbacks of deepsea fish oil due to the hydrophilic and oleophilic properties of nanolotion.

Keywords: Nano lotion, Deep sea fish oil, Extraction, Food industry.

1. Introduction

Nowadays, consumers view health from a broader and more complex perspective, prioritizing food safety and nutritional health, which has also led to the rapid appreciation of the health product market, among which deep sea fish oil is a very popular health food for teenagers, as well as elder people. Deep sea fish oil can promote cardiovascular health and prevent cardiovascular diseases such as cerebral thrombosis, cerebral hemorrhage, hypertension, and myocardial infarction. For children, it can promote brain development, mature retinal photoreceptor cells, and enhance brain cell development. It can even alleviate mental illnesses, treat joint pain, and so on [1].

At present, the health market has exceeded $1.5 trillion, with an annual growth rate of 5% to 10% [2]. Among which, fish oil accounts for 0.69% of the total health market [3]. It can be seen that people nowadays attach great importance to nutrition and health, and fish oil is an important choose for healthy products.

While fish oil brings benefits to people, there are still large challenges in the administration process of Deep sea fish oil, mainly include poor absorption rate, and high cost in purification.

DOI: 10.54254/2753-8818/2025.AU27426

For poor absorption rate, Poor absorption rate causes: high taking dose; advert effect; cardiovascular. At present, most fish oil products are in capsule form and lack appropriate packaging technology, which makes it difficult for the active substances in fish oil to be absorbed, and the generated oxides can also harm the human body. Causing various side effects in the human body due to excessive intake of fish oil. If taking high doses of fish oil, diarrhea and bloating may occur due to stomach discomfort. Secondly, due to the high concentration of fat, there may be acid reflux in the stomach. The main symptoms include heartburn, hiccups and stomach discomfort. Fish oil may even cause symptoms such as low blood pressure and high blood sugar. Thirdly, excessive consumption of fish oil in pursuit of effectiveness may not prevent blood clots and instead increase the likelihood of bleeding [4]. Most seriously, once a person slightly overdoses deep-sea fish oil, omega-3 will cause arrhythmia, and the incidence rate is as high as 37%. These side effects result in many people who need deep-sea fish oil being unable or not recommended to take fish oil due to their own symptoms such as obesity, high blood sugar, and low blood pressure [4].

Besides, purification efficiency of fish oil is very low, which not only improves the cost, but also easily permit the advert product with toxicity into the final product of fish oil. Meanwhile, the purification of fish oil is also a huge challenge. The fish oil purified by traditional methods not only has high cost and low efficiency, but also generates toxic oxides to the human body and even pollutes the environment. So we urgently need to use new technologies to purify deep-sea fish oil [5].

Nano technology has been rapidly used in advancing the food industry, demonstrating great potential. For example, nanocapsules in the nano delivery system (used for food packaging technology) have been widely used in the packaging of functional food, and nano lotion, one of the current research hotspots, is very effective in maintaining the active ingredients in food. In order to address these issues and benefit more people who need fish oil and other functional factors, this thesis studied the possibility of applicating nanotechnology to the industry production of deep sea oil, to improve the purification efficiency, as well as the absorption rate.

2. Overview of nanotechnology in food industry

Nanotechnology is a scientific technology that utilizes individual atoms and molecules to manufacture substances, studying the properties and applications of the structural dimensions (a space composed of length, width, and height, with at least one dimension of length, width, and height) of materials within the range of 1-100 nanometers. Nanotechnology includes the design, research, manufacturing, and control of shape and size of nanoscale materials.". At the same time, nanoscale technology can more precisely control items, perform more careful and accurate controllable operations on raw materials, place, model, measure, and produce, thereby changing the properties and functions of substances at the atomic level. Nanotechnology covers a wide range of fields, including colloid science, chemistry, biology, physics, and other fields, including the study of nanoscale phenomena [6].

2.1. Advantage of nanotechnology

Based on previous research, the advantages of nanoparticles are greater chemical and biological activity, enzyme reactivity, permeability, catalytic behavior, and quantum properties. This is because the ratio of surface area to mass transfer rate of nanoparticles is the same as that of large particles, while nanoparticles have a much smaller surface area than large particles, so they are superior in quantity. This also means that nanoparticles have a powerful role in improving material properties.

DOI: 10.54254/2753-8818/2025.AU27426

The essence and promising development prospects of nanotechnology, as well as the superiority of nanoscale materials, are all based on a theoretical foundation. This theory suggests that the properties of nanoscale materials may be completely different from those of other materials of the same type. In other words, when the size of the same material is reduced to below 100 nanometers, its physical and chemical properties will undergo significant changes. Research has shown that these changes are often benign, meaning that nanomaterials have stronger properties and effects than bulk materials in all aspects. This directly establishes the significant technological pursuit of nanotechnology in many industrial and scientific research fields [6].

2.2. Application of nanotechnology in food industry

Nowadays, nanotechnology has been already widely used in food industry, including food processing, food packaging, food preservation, et al. The discovery of nanoscale new materials, phenomena, and processes, as well as the advancement of new theoretical and experimental research technologies, provide new opportunities for the development of nanostructured materials and nanosystems.

For food processing, nanotechnology is being widely applied in functional food processing research. Nanoparticles are often used as food additives to protect food from contamination and extend its lifespan. Because nanomaterials have three major characteristics: higher barrier properties, wider surface area to volume ratio, and higher antibacterial efficacy, they help overcome the shortcomings of traditional methods for extending shelf life. Nanotechnology also aims to solve food related diseases (such as diabetes and obesity), develop specific nutritional diets for different populations, especially the elderly, and diseases caused by some unhealthy lifestyles, and maintain the quantification and sustainability of their production. This technology ensures the creation of devices for targeted delivery of nutrients through nutritional nanotherapy [7].

Based on the important role of nanotechnology in food safety and nutrition, we also speculate that nanotechnology has enormous potential in developing new safe nutritional products. Therefore, we attempt to discuss the feasibility of improving deep-sea fish oil products with obvious advantages and numerous disadvantages through nanotechnology.

2.3. Overview of deep sea fish oil

There are three functional factors in deep-sea fish oil, namely Omega-3 polyunsaturated fatty acids, docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA). Research has shown that Omega-3 polyunsaturated fatty acids can effectively prevent cardiovascular disease without excessive intake. Omega-3 fatty acids are mainly composed of eicosapentaenoic acid and docosahexaenoic acid at the microscopic level, with long chains of approximately 18-22 carbon atoms. The biggest characteristic of omega-3 polyunsaturated fatty acids is their highly curved structure. This structure is due to the natural presence of many double bonds in fatty acids, which are in a "cis" configuration, causing the fatty acid structure to fold and lower its melting point, allowing it to maintain high-speed liquid flow at lower temperatures (referring to room temperature of 23 degrees Celsius). Due to this characteristic, small amounts of omega-3 fatty acids do not solidify into solids in the human body, posing a danger to the body [8].

DHA and EPA functional factors are mainly present in marine mammals, with fish oil and seal oil having the highest content (about 5% of total fatty acids). Its structure is similar to Omega-3 fatty acids [8].

DOI: 10.54254/2753-8818/2025.AU27426

Deep sea fish oil has very powerful effects on preventing and even treat many chronic diseases, especially microvascular diseases. As this thesis discussed before, deep sea fish oil is rich in omega-3 unsaturated fatty acids and two functional factors, DHA and EPA, which effectively protect the health of cells and the brain, by controlling inflammation and reducing the probability of inflammation. Moreover, omega-3 fatty acids have the highest reserves in fish oil, so although there are also small amounts of omega-3 fatty acids in ingredients such as nuts, avocados, and vegetable oils, most people still choose to directly consume deep-sea fish oil [9]. Except for controlling systematic inflammation in human body, research has found that if heart disease patients take fish oil every day for six months, their condition improves, manifested by reduced scars on the myocardium and reduced inflammation symptoms. Therefore, deep-sea fish oil can reduce the incidence of heart disease and alleviate the condition of cardiovascular disease [9]. Besides, Deep sea fish oil can also remove unhealthy cholesterol from the blood, and protects human body from cardiovascular diseases. In a study published in December 2017, it was shown that patients with hyperlipidemia significantly reduced their total cholesterol and triglyceride levels after taking fish oil for eight consecutive weeks.

Deep sea fish oil can also promote brain development for both teenagers and elderly people. Many parents encourage their children to take fish oil, and elderly people who have normal cognitive function are suggested to persistently take fish oil. As they age, their cognitive decline rate is significantly lower than other elderly people. What's more, Fish oil can also improve sleep quality. A study in the Journal of Nutrition suggests that fish oil can enhance the secretion of melatonin, a hormone that improves sleep quality and regulates sleep cycles. Taking 600 milligrams of fish oil daily for 16 consecutive weeks can effectively improve a child's sleep quality. So these two benefits also mean that deep-sea fish oil may be able to inhibit rapid aging. Elderly people with good physical health, clear cognition, good sleep quality, and good mood often live longer [10].

2.4. Current purification process of deep sea oil in industry

The traditional extraction of fish oil involves extracting triacylglycerol, which is made from fish and fish by-products. The main step is to boil the fish raw materials, crush or press them with stones, and then obtain crude fish oil through filtration or centrifugation. But this method has strong oxidation sensitivity, high melting point, thermal sensitivity, hydrophobicity, and other drawbacks. In the extraction process, fish oil is easy to form oil-water lotion, which reduces the efficacy of fish oil and increases the risk of excessive consumption. Moreover, this oil-water lotion is very stable and can hardly be separated by filtration or centrifugation. In addition, omega-3 unsaturated fatty acids in fish oil have long chains with double bonds, making them unstable at high temperatures. They oxidize most of the fatty acids, reducing the efficacy of fish oil while also generating harmful peroxides such as aldehydes, ketones, acids, esters, and alcohols.

Organic solvent extraction is another conventional technique. The most important step of this technology is to remove water from organic solvent, so as to prevent the difficulty in separating lotion due to the inability to remove water through compression, cooking and crushing, and grind while removing water. This method effectively solves the problem of hydrophobicity in fish oil (extracting all the water), but other problems have not been solved, including highly oxidizable and high melting point, and this method has a long pre-treatment period, which greatly increases the cost. And the natural toxicity of organic solvents also hinders the popularization of this method [11].

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2.5. Market situation of deep sea fish oil

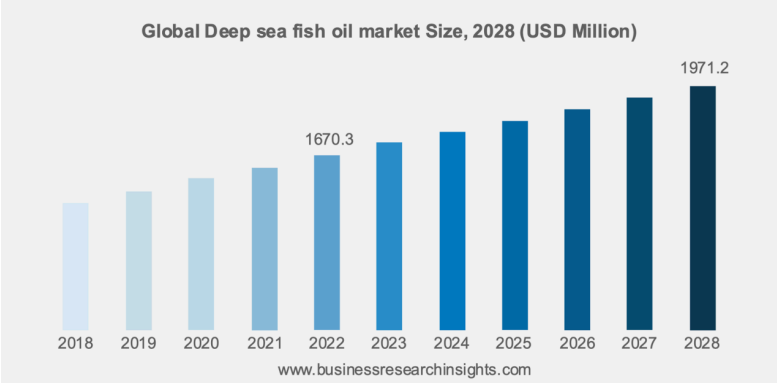

Figure 1. Fish oil market size

In Figure 1, we can find in 2022, the global deep-sea fish oil market is expected to reach $1.6703 billion and is projected to reach $1.9712 billion by 2028, with a compound annual growth rate of 2.8% during the forecast period. Despite the impact of the global COVID-19 epidemic, the total market value of fish oil has not been greatly affected, but has been rising steadily. This shows fish oilis widely acknowledged to promoting people's health.

Deep sea fish oil has its unique role in various fields, so its market is constantly expanding. Deep sea fish oil is rich in beneficial compounds such as omega-3 fatty acids, which are not limited to dietary supplements and can provide a more comprehensive nutritional supplement for the human body. It is increasingly being applied in various fields, including pharmaceuticals, functional foods, cosmetics, and pet nutrition. In the pharmaceutical industry, it is a cardiovascular and cognitive health drug. In the food industry, it is used to enhance products such as dairy products, grains, and infant formula. The cosmetics industry is leveraging its anti-aging and skin health properties [12]. Even the pet nutrition department recognizes its benefits for animal health. As various industries continue to explore innovative methods of integrating deep-sea fish oil into their products, the market for deep-sea fish oil will continue to expand, attracting a wider customer base and stimulating the market.

2.6. Unmet medical needs in the market of deep sea fish oil

Despite the powerful effects of fish oil, there are still large unmet medical needs in the market of deep sea fish oil, mainly including improvement of poor absorption rate, and optimization of purification process. Firstly, fish oil has extremely poor water solubility and low solubility, mainly due to high levels of PUFA in fish oil. This also leads to the inability of the human body to absorb fish oil very effectively. Excessive waste of fish oil can pose a risk of poisoning if it accumulates in the human body. At the same time, deep-sea fish oil also has unpleasant disadvantages such as oxidation sensitivity and high melting point. This also directly hinders their application in the food industry, as blindly adding fish oil to food can cause unpredictable harm to the human body. The last and most dangerous point is the presence of toxic compounds such as ketones and aldehydes produced by oxidation in deep-sea fish oil, which limits its widespread application.

Further more, the benefits of deep-sea fish oil on the human body can also evolve into drawbacks. For instance, deep-sea fish oil has been proven to prevent heart disease and coronary heart disease, reduce the frequency of cardiovascular disease attacks and the risk of death. But some

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researchers have expressed concerns about the possibility of frequent triggering of atrial fibrillation (a-fib) by deep-sea fish oil. Atrial fibrillation is an arrhythmia, where the upper chamber of the heart changes from effective contraction to chaotic vibration. In an analysis of the past five clinical trials conducted by the European Heart Journal in April 2021, researchers found that patients taking drugs containing Omega-3 fatty acids had a 37% higher frequency of developing atrial fibrillation compared to patients receiving a placebo. In these studies, the daily intake of deep-sea fish oil was only between 0.84 grams and 4 grams. Although a-fib does not immediately endanger life, it may lead to complications such as heart failure or stroke. However, the American Heart Association recommends eating two servings of fish per week to reap the benefits of fish oil. So, we need more research to fully understand the relationship between prescription fish oil and a-fib. Speaking of fish oil, it is not completely perfect. Taking this supplement carries certain risks [13].

These are unmet medical or healthcare needs for fish oil. However, it is gratifying to note that in recent years, utilizing food grade delivery systems to transport DHA/EPA and enhance its biological efficacy has become an attractive method with fascinating prospects. This review focuses on the potential delivery systems of DHA/EPA, including micro lotion, nano lotion, Pickering lotion, hydrogel, lipid particles, oil gel, liposome, microcapsule and micelle.

3. Discussion on application of nanotechnology on fish oil usages

At present, most of the applications of deep-sea fish oil in capsules or functional foods are still in the packaging technology. However, directly introducing fish oil or active ingredients from fish oil into functional foods or supplements still faces significant challenges. For example, fish oil capsules using nano encapsulation technology have emerged, but omega-3, DHA, or EPA nanoparticles are rarely seen.

Nowadays, Gorbanzad et al. have achieved the technology of using nanoliposomes to enhance nano encapsulated fish oil. This refers to their use of nanoparticles to add polyphenols, volatile additives, pigments, enzymes, and bacteria to small capsules during the preparation and extraction of fish oil capsules, in order to stabilize, protect, and preserve them from processing, nutritional, and health losses. So the use of nanoliposome encapsulation technology can enable the large-scale production of lipophilic materials using natural ingredients, such as deep-sea fish oil and its active ingredients. And Gorbanzad et al. have achieved the delivery of active ingredients from fish oil into yogurt, making it a functional food with fish oil effects [9].

3.1. Improvement of the bioavailability of functional foods using nanocapsule encapsulation technology

Nanocapsules are currently a widely used technology in the food industry and are very popular in the field of food research. Nanocapsules are materials that package active ingredients in solid, liquid, or gaseous form through natural or synthetic polymers. The advantages of nanocapsules are small volume, easy suspension in water, good dispersibility, which is conducive to the formation of uniform and stable colloidal solutions. Also, it has good targeting and sustained release effects. If nanocapsules are applied to the development of new functional foods, especially by embedding functional factors into functional food containers, they can effectively reduce the loss of functional factors during processing or storage, and help transmit functional factors to the gastrointestinal tract without damage, and then be absorbed by the human body. The specific targeting of nanocapsules can alter the distribution of functional factors and concentrate them in specific target tissues, thereby achieving the goal of reducing toxicity and improving therapeutic efficacy. By controlling the

DOI: 10.54254/2753-8818/2025.AU27426

release of functional factors, its bioavailability can be improved. Now, research results on more stable liposome packaged nanocapsule delivery systems have emerged, which makes the functional foods processed by nanocapsule delivery systems more stable and antioxidant, laying the foundation for the study of functional active substance drug delivery systems. At present, there are health products with nanocapsules on the market, and their application in new functional foods and commercialization is just around the corner. However, the disadvantage of nanocapsules is that their intelligent application in packaging technology does not solve the problem of functional factors from the fundamental steps of purification and preparation [14].

Nano lotion is the focus of research on new functional food. Compared with nanocapsules, nano lotion has broken the limitation that it can only be used for packaging technology. In theory, nano lotion can participate in the purification and preparation of active ingredients in functional foods, fundamentally improving the active ingredients and removing substances harmful to human health. Nano lotion is also widely used. It is highly effective for fat soluble materials such as deep-sea fish oil, but not completely ineffective for water-soluble materials. Because the characteristic of nano lotion is that both water phase and oil phase are possessed, and its essence is oil-water mixture. This leads to its good performance in both fat soluble and water-soluble materials. This makes the active ingredients in functional foods easy to absorb, effectively avoiding the phenomenon of absorbing other substances. At the same time, the nano lotion has better stability and more uniform size than the traditional lotion, and avoids particle aggregation caused by gravity. Secondly, the surfactant in the nano lotion is a biocompatible biological macromolecule, and its dosage is very small. At the same time, the content of organic cosolvent in nano lotion is very low, which can effectively improve the production efficiency. However, nano lotion is toxic and cannot be ignored. The small size effect of nano detergents enables them to quickly pass through the gastrointestinal barrier and cellular tissues, so additional substances used for transporting active substances may accumulate in human tissues. At present, researchers are unable to predict whether they will react with other substances and pose potential safety risks. This is why nano lotion is still under research and has not been put into the market [14].

3.2. Other Nano delivery systems which has the potential to be used in fish oil

Nanomicelles belong to nanodispersion systems because they are typically in liquid form with almost no oil phase, making them almost ineffective for lipid soluble materials. On the contrary, nanoliposomes are a biofilm structure composed of phospholipids and cholesterol. The overall appearance is in the form of closed vesicles. And precisely because nanoliposomes are essentially nanolipid particles, solid, they are almost insoluble in water and have no effect on water-soluble materials. Two nanometer lotion neutralizes the shortcomings of these two nanotechnology and forms more stable and efficient nanomaterials [14].

Nano nutritional additives. The most common ones are nano selenium, nano iron, nano zinc, and nano calcium. Nano trace element additives are new active ingredients obtained by nano processing essential trace elements for the human body, which can improve their physicochemical properties, solubility, antioxidant activity, retention and release time, and gastrointestinal stability. This method can enhance the utilization and absorption of trace elements in food in the body, improve its bioavailability and safety [14].

DOI: 10.54254/2753-8818/2025.AU27426

3.3. Application examples of nano delivery systems in functional foods and comparison with deep-sea fish oil

Ginger contains a large amount of curcumin, which helps to manage oxidative and inflammatory conditions and slow down the onset of some inflammations when absorbed by the human body. Curcumin can also improve metabolic syndrome, arthritis, anxiety, and hyperlipidemia. For athletes, curcumin, which can treat inflammation and muscle soreness caused by intense exercise, is a necessity in daily life. So the common feature between curcumin, an active ingredient, and deep-sea fish oil is its low melting point, difficulty in extraction, as well as its tendency to oxidize and poor water solubility. After applying nano micelles to the production of curcumin, Chen et al. found that the solubility of curcumin nanoparticles was 1000 times higher than that of free curcumin molecules, and they were not damaged under light and high temperature conditions. By testing the drug loading rate, stability, and release rate, the excellent performance of nano curcumin has been demonstrated. Based on this, we can speculate that deep-sea fish oil can also use nanomicelle delivery systems to enhance its performance and improve its disadvantages of easy oxidation and strong hydrophobicity.

Active ingredients with properties similar to deep-sea fish oil include not only curcumin, but also natural plant-based pigments such as lutein and carotenoids. Their common characteristics are poor water solubility stability and susceptibility to oxidation. At present, nano lotion has been used to construct nano transfer system to carry, store, transfer and even control the release of active ingredients. As the carrier of high content of bioactive ingredients, nano lotion can enhance the water solubility and oil solubility of bioactive ingredients, thus improving the dispersibility and bioavailability of substances. Rao et al. found that the micro lotion can carry and evenly distribute functional factors in food by preparing food grade micro lotion. This effect is more pronounced in fat soluble ingredients and foods. Deep sea fish oil is fat soluble, so we can also speculate that nano lotion will play a great role in the preparation of deep sea fish oil. Afterwards, Zhang et al. generated ions through the interaction of static electricity and hydrogen bonding, and obtained self-assembled colloidal nanoparticles. This nano particle and white oil form a nano lotion with more powerful emulsification performance, and improve the stability of the micro lotion. Later, Jalali, Roohinejad and others successfully used this oil in water ion nano lotion to extract lutein and carotene, and found that their oxidizability, hydrophobicity and other properties were significantly improved. Therefore, we can judge that it is feasible and even the most effective way to use nano lotion to build a nano transport system to prepare deep-sea fish oil [15].

4. Conclusion

Through the study, organization, and comparison of various literature, this study first discovered that deep-sea fish oil currently has significant medical needs that have not been met and its own shortcomings, such as high melting and boiling points, susceptibility to oxidation, and hydrophobicity. These drawbacks also lead to many people experiencing side effects without proper precautions, posing a threat to human health. Then, this article found that nanotechnology may be helpful in improving the physicochemical properties of deep-sea fish oil. Nano encapsulation technology has successfully improved deep-sea fish oil during the packaging stage. The study found that the nano lotion technology can theoretically improve the hydrophobicity, oxidizability and other shortcomings in the purification process of deep-sea fish oil. For this reason, this study compared various literature on the research of new healthy functional foods through nano technology, and

DOI: 10.54254/2753-8818/2025.AU27426

found that it is really feasible to improve the physical and chemical properties of deep-sea fish oil by using nano lotion technology.

In future research, people may really add nano lotion to the preparation of deep-sea fish oil, or perfectly solve the problem of oxide toxicity of Omega-3 fatty acids, which can greatly reduce the side effects of deep-sea fish oil, or further improve the bioavailability of deep-sea fish oil by integrating nanotechnology with other materials or technologies. In the future, nanotechnology can play a significant role in deep-sea fish oil and even in the entire food safety and food industry.

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